The case of the missing neutrality

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Abstract. The concept of neutral evolutionary networks being a significant factor in evolutionary dynamics was first proposed by Huynen *et al.* about 7 years ago. In one sense, the principle is easy to state — because most mutations to an organism are deleterious, one would expect that neutral mutations that don't affect the phenotype will have disproportionately greater representation amongst successor organisms than one would expect if each mutation was equally likely.
So it was with great surprise that I noted neutral mutations being very rare in a visualisation of phylogenetic trees generated in *Tierra*, since I already knew that there was a significant amount of neutrality in the Tierra genotype-phenotype map. The paper reports on an investigation into this mystery.

1 Introduction

The influence of *neutral networks* in evolutionary processes was first elucidated by Peter Schuster's group in Vienna in 1996[4,6]. Put simply, two *genotypes* are considered *neutrally equivalent* if they map to the same *phenotype*. A *neutral network* is a set of genotypes connected by this neutrality relationship on links with Hamming distance 1 (ie each link of the network corresponds to a mutation at a single site of the genome).

These researchers noted that evolution tended to proceed by diffusion along these neutral networks, punctuated occasionally by rapid changes to phenotypes as an adaptive feature is discovered. The similarity of these dynamics with the theory of Punctuated Equilibria[3] was noted by Barnett[2]. It was also noted that if a *giant network* existed that came within a hop or two of every possible genotype, evolution will be particularly efficient at discovering solutions.

Most work on neutrality in evolution uses the genotype-phenotype mapping defined by folding of RNA[7]. This mapping is implemented in the open source Vienna RNA package[1], so is a convenient and well known testbed for ideas of neutrality in evolution.

Also in 1996, I developed a definition of the genotype-phenotype mapping for Tierra, which was first published in 1997[8]. I noticed the strong presence of neutrality in this mapping at that time, which was later exploited to develop

[1] http://www.tbi.univie.ac.at/~ivo/RNA

a measure of complexity of the Tierran organism[11,9]. In 2002, I started a programme to visualise Tierra's phylogenetic trees and neutral networks[10] in order to "discover the unexpected". Two key findings came out of this: the first being that Tierra's genebanker data did not provide clean phylogenetic trees, but had loops, and consisted of many discontinuous pieces. This later turned out to be due to Tierra's habit of reusing genotype labels if those genotypes were not saved in the genebanker database. This might happen if the population count of that genotype failed to cross a threshold. This is all very well, except that a reference to that genotype exists in the parent field of successor genotypes. The second big surprise was the paucity of neutral mutations in the phylogenetic tree. We expect most mutations to an organism to be deleterious, and so expect that neutral mutations will have disproportionately greater representation amongst successor genotypes than one would expect if each mutation was equally likely.

2 Neutrality in Tierra

Tierra[5] is a well known artificial life system in which small self-replicating computer programs are executed in specially constructed simulator. These computer programs (called digital organisms, or sometimes "critters") undergo mutation, and radically novel behaviour is discovered, such as *parasitism* and *hyperparasitism*.

It is clear what the genotype is in Tierra, it is just the listing of the program code of the organism. The phenotype is a more diffuse thing, however. It is the resultant effect of running the computer program, in all possible environments. Christoph Adami defined this notion of phenotype for a similar artificial life system called *Avida*[1]. In Avida, things are particularly simple, in that organisms either reproduce themselves at a fixed replication rate, or don't as the case may be, and optionally perform range of arithmetic operations on special registers (defined by the experimenter).

In Tierra, organisms do interact with each other via a template matching mechanism. For example, with a branching instruction like `jmpo`, if there is a sequence of `nop0` and `nop1` instructions (which are nooperations) following the branch, this sequence of 1s and 0s is used as a template for determining where to branch to. In this case the CPU will search outwards through memory for a complementary sequence of `nop0`s and `nop1`s. If the nearest complementary sequence happens to lie in the code of a different organism, the organisms interact.

To precisely determine the phenotype of a Tierran organism, one would need to execute the soup containing the organism and all possible combinations of other genotypes. Whilst this is a finite task, it is clearly astronomically difficult. One means of approximation is to consider just interaction of pairs of genotypes (called a tournament). Most Tierran organisms interact pairwise — very few triple or higher order interactions exist. Similarly, rather than running tournaments with all possible genotypes, we can approximate matters by using the genotypes stored in a genebanker database after a Tierra run. In practice, it turns out that various measures, such as the number of neutral neighbours, or

the total complexity of an organism are fairly robust with respect to the exact set of organism used for the tournaments.

So the procedure is to pit pairwise all organisms in the genebanker against themselves, and record the outcome in a table (there is a small number of possible outcomes, which is detailed in [8]). A row of this table is a phenotypic signature for the genotype labeling that row. We can then eliminate those genotypes with identical signatures in favour of one canonical genotype. This list of unique phenotypes can be used to define pragmatically a test for neutrality of two different organisms. Pit each organism against the list of unique phenotypes, and if the signatures match, we have neutrality. The source code for this experiment is available from the author's website.[2]

Tierra has three different modes of mutation:

Cosmic Ray A site of the soup is randomly chosen and mutated;
Copy Data is mutated during the copy operation;
Flaw Instructions occasionally produce erroneous results

Furthermore, in the case of cosmic ray and copy mutations, a certain proportion of mutations involve bitflips, rather than opcodes being substituted uniformly. This proportion is set as a parameter in the soup_in file (`MutBitProp`) — in these experiments, this parameter is set to zero.

In order to study the issue of whether neutrality is greater or less than expected in Tierra, I generated three datasets with each of the 3 modes of mutation operating in isolation. The sizes of each data set was 69,139, 87,003 and 198,982 genotypes respectively, generated over a time period of about 1000 million executed instructions. Genebanker's threshold was set to zero, so all genotypes were captured. This led to a proper phylogenetic tree. After performing a neutrality analysis, a set of 83, 86 and 158 unique phenotypes was extracted as the test set for the tournaments.

Since the neighbourhood size increases exponentially with neighbourhood diameter, I restrict analysis to single site, or point mutations. In each data set, around 7% of these genotypes were created were created by a mutation at a single site and were neutrally equivalent to its parent. For each of these, I compute the number of neutral neighbours n_i existing in the 1 hop neighbourhood of the parent genotype i, which is of size 32^{ℓ_i}, where ℓ_i is the length of the genome. For a given parent i, the ratio

$$r_i = \frac{\nu_i 32^{\ell_i}}{o_i n_i} \tag{1}$$

gives the proportion of neutral links actually followed relative to the number of neutral links available (*neutrality excess*), where ν_i is the number of neutrally equivalent offspring, and o_i the total number of offspring and the size of the 1 hop neutral neighbourhood. Fig. 1 shows the running average of this quantity over these transitions, with the genotypes numbered in size order.

[2] http://parallel.hpc.unsw.edu.au/getaegisdist.cgi/getsource/eco-tierra.3, version 3.D3

In this analysis, no selection is operating, so one would expect that the neutrality excess should be identical to 1. However, in the case of instruction flaws, it is rather unpredicatable what the effect is. In the case of cosmic ray mutations, 50% of time one would expect the parent to be mutated, rather than the daughter. In the case of a mutation affecting a crucial gene of a parent genotype, the organism may not be able to reproduce at all, thus favouring neutral mutations. Only copy mutations should affect all sites of the genome equally, leading to a neutrality excess equal to one. The measured value, however is about 1.3, substantially greater than one. The reason for this is not known at this point in time.

The the datasets were further subsetted to include just those transitions whose daughter organism successfully reproduced, ie with a maximum population count greater than 1. The neutrality excess in this case is substantially less than 1, so something in Tierran evolution is favouring nonneutral evolution.

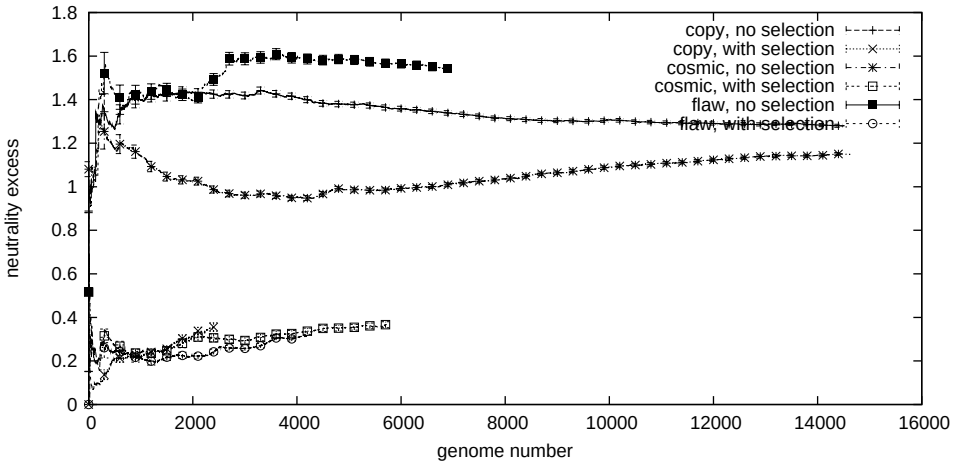

Fig. 1. Running average of neutrality excess ($\langle r_i \rangle$). Genomes are ordered according to size, and neutrality excess is averaged over all genomes to the left of that data point. Three different datasets are analysed, with each of the three modes of mutation turned on. Then the datasets are further filtered to only include offspring whose maximum population count is greater than 1, ie selection is operating.

3 Vienna RNA folding experiments

It is quite well known that evolution using the RNA folding map[7] exhibits a great deal of neutrality, at least for a standard genetic algorithm optimising a well defined fitness function. Tierra is a coevolutionary system, and does not

have a well defined fitness function. Rather, the chance of an organism surviving at each time step depends on what other organisms are in the environment at the time, and has a significant component of contingency.

One possible cause for the repression of neutrality in Tierra is this coevolutionary nature. The reasoning follows from the idea of the *Red Queen effect*[12]. This says that organisms must continuously evolve just to remain adaptive.[3] In such a circumstance, neutral evolution is maladaptive, and surely be suppressed.

A convincing argument in favour of this hypothesis would be the demonstration of a coevolutionary system based on the RNA folding map that exhibited this repression of neutrality. Whilst I haven't achieved this goal, I will report on a couple of attempts.

The first attempt is an instantiation of the simplest possible coevolutionary system. It consists of two populations: a tracker population T which attempts to be as similar to the other population as possible, and an evader population E that attempts to be as different from the tracker population as possible. The Vienna RNA folding library is used, and fitness functions $f_T(x, E)$, $f_E(x, T)$ defined for the trackers and evaders respectively, based on the average distance between their phenotypes:

$$f_T(x, E) = -\frac{1}{N_E} \sum_{y \in E} d(x, y), \; \forall x \in T$$
$$f_E(x, T) = \frac{1}{N_T} \sum_{y \in T} d(x, y), \; \forall x \in E \tag{2}$$

where N_T and N_E are the population counts of trackers and evaders respectively, and $d(x, y)$ is the *string edit distance*[4] between the folded structure of x and y.

I implemented a simple genetic algorithm with just a point mutation operator. All RNA strings have the same length. During reproduction, each RNA string copies itself, possibly with a mutation. During the selection step, the least fit 50% of organisms are culled, bringing the population count back to the starting value. For the results presented in Fig. 2, the GA parameters are shown in Table 1. Source code for this experiment is available from the author's website.[5]

String length:	20
Population size:	100
Mutation probability per site:	0.1

Table 1. Genetic Algorithm parameters for the RNA folding experiment reported in the paper

[3] Like the Red Queen in Lewis Caroll's *Through the Looking Glass*, who had to keep running, just to stay where she was.

[4] Please consult the Vienna RNA package documentation for a precise definition of string edit distance

[5] http://parallel.hpc.unsw.edu.au/getaegisdist.cgi/getsource/rnafold/, version D1

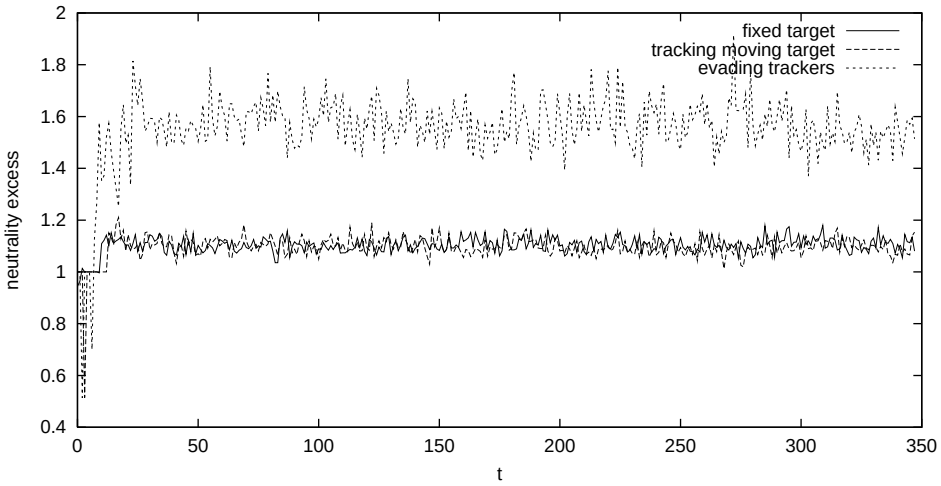

Fig. 2. Neutrality excess for the RNA folding experiment, as a function of time. Separate lines are plotted for trackers, evaders and trackers tracking a fixed target.

Fig. 2 shows the neutrality excess for trackers and evaders, defined in the same way as eq (1). A third baseline run of a single population tracking a fixed target is also shown (corresponding to a classic fixed fitness function genetic algorithm). The most obvious thing about these results is that neutrality is highly adaptive to evaders, who clearly are trying to make themselves occupy as small a footprint in phenotype space as possible. Given the evaders propensity to stay still, trackers will tend to behave like their fixed target counterparts.

This indicated that trackers were dominating over the evaders. Another experiment I performed was where all coevolving populations were symmetric. In this case, each population would track a second and evade a third population. The simplest arrangement of these has 3 coevolving populations in a "Rock, Scissors, Paper" configuration, so no one population dominates. I also tried other combinations up to 10 separately coevolving populations, wired up randomly to each other (but fixed at the start of the experiment). In all cases, the results were much the same — the neutrality excess was less than for the trackers in Fig. 2, but still just slightly greater than 1.

So how do can we introduce the Red Queen effect to this system? One possibility I haven't explored as yet is to somehow give evaders room to move, perhaps by including a genome lengthening operator as part of the GA.

4 Conclusion

The suppression of neutrality in Tierran evolution is a real effect. It is quite likely that this is a Red Queen effect, with organisms needing to change to remain adaptive. Experiments with using the RNA folding map to try to reproduce this

effect have proven inconclusive. However, it was noted that there is significant evolutionary pressure to increase neutrality in evading populations.

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